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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/776,780	DURING, MATTHEW J.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12,14-16,18 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-12,14-16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/10/04 & 9/8/06* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed September 8, 2006 (hereinafter referred to as "the response") has been entered. Claims 1, 5, 12, 15, and 16 have been amended. Claims 3, 13, and 17 have been cancelled.

Accordingly, Claims 1, 2, 4-12, 14-16, 18, and 19 remain pending in the instant application.

The objections to Figures 2 and 7 are withdrawn in view of the replacement drawings filed 9/8/06.

The objection to the specification for failing to capitalize the trademarks NEUROBASAL and MINI COMPLETE is withdrawn in view of the amendments to the specification at pages 47 and 49.

The objection to the specification regarding the Brief Description of the Drawings for Figure 6H is withdrawn in view of the amendment to the specification at page 8.

The objection to the specification regarding the Brief Description of the Drawings for Figures 7A-7B is withdrawn in view of the amendment to the specification at page 8.

The objection to the specification regarding the Brief Description of the Drawings for Figures 12-12C is withdrawn in view of the amendment to the specification at page 10. The objection to the Brief Description of Figure 12D remains, as set forth hereinbelow.

The objection to Claim 5, regarding the misspelling "stoke", is withdrawn in view of the amendment to the claim.

The rejection of Claims 1, 2, 5-12, and 15-19 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is withdrawn in view of the amendments to the claims to now recite a nucleic acid sequence encoding an NMDA receptor antigen and further in view of the cancellation of Claim 17.

The rejection of Claims 1, 3, 4, and 7-11 under 35 U.S.C. 112, second paragraph, for indefiniteness in their recitation of "excessive neuronal activity," is withdrawn in view of the amendment to Claim 1 to remove the phrase "excessive neuronal activity."

The rejection of Claim 15 under 35 U.S.C. 112, second paragraph, for lack of antecedent basis for the limitation "neurological disorder", is withdrawn in view of the amendment to Claim 12 to recite a "neurological disorder."

The rejection of Claim 15 under 35 U.S.C. 112, second paragraph, for lack of antecedent basis for the "genetic vaccine of claim 12", is withdrawn in view of the amendment to Claim 15 to recite "the method of claim 12."

Drawings

The drawings remain objected to under 37 CFR 1.83(a) because they fail to show the histological details as described in the specification. Specifically, the resolution and clarity of Figures 3, 4, 7-10, and 13 are so poor as to make it impossible to discern the structural details. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either

"Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). The label should be placed in the top margin (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The replacement drawings submitted September 8, 2006 are acknowledged. As for Figures 3, 4, 7-10, and 13, however, the resolution is no better than the originally filed drawings.

Specification

The disclosure is objected to because of the following informalities:

The Brief Description of the Drawings refers to Figures 2A-2H, but there is no description of Figures 2E-2H.

The explanation at page 9 of the response does not resolve the deficiency. Applicants assert that the figures are described at page 55, line 17 through page 56, line 8 of the specification, but the cited section does not refer to Figures 2E-2H. Thus, the specification remains deficient.

The Brief Description of the Drawings refers to different rat groups in Figure 12D, but it cannot be determined which bars represent each particular rat group.

The assertion at page 9, paragraph 4 of the response and the amendment presented at page 2 of the response do not resolve the deficiency because the labelling of the X-axis conflicts with the labelling of the individual bars and the amendment to the specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-12, 14-16, 18, and 19 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a neurological vaccine comprising an AAV vector encoding NMDAR1 and a method of ameliorating brain damage associated with epilepsy or stroke in a rat, via prior oral administration of said vaccine, does not reasonably provide enablement for a neurological vaccine comprising any vector encoding any NMDA receptor antigen for treatment of any injury or disease, and a method of modulating a neurological disorder in any subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of enablement set forth above is not intended to suggest specific claim language, but rather is intended to advise Applicant of the broadest scope that is considered to be enabled. It is Applicant's responsibility to identify claim language that is properly supported in the specification and that falls within the scope acknowledged to be enabled.

At pages 10-11 of the response, Applicant asserts that the claims are now directed to a vaccine comprising a specific antigen, an NMDA receptor antigen, and provides a specific effect, neuroprotection. However, requiring "neuroprotection" is no more specific than "[improving] the neurological condition." In fact, the term seems broader, at least in the sense that it now covers "neuroprotection" in healthy animals that have no "neurological condition." As set forth in the original claim construction, while the metes and bounds were not clearly set forth, at a minimum, an improvement in the neurological condition was required, whereas the term "neuroprotection" embraces situations where no further deterioration is observed. For at least these reasons, it is maintained that the claims continue to cover treatment of any neurological injury or disease. Applicant further asserts that "the expressed antigen elicits production of antibodies," but the claims in their present form do not require expression of the antigen, nor does the vaccine composition include any regulatory elements necessary for expression to occur. Applicant goes

on to discuss the mechanism by which the claimed invention is believed to work. The response does not, however, address the unpredictability inherent to the art of DNA vaccination.

At page 11 of the response, Applicant asserts that the Examiner is attempting to limit the scope of Applicant's claims to cover only the embodiments disclosed in the working example. However, a complete *Wands* analysis has been provided, with a discussion of those factors most relevant to the present claims, including the nature of the invention, the state of the prior art, the predictability of the art, the breadth of the claims, the amount of direction or guidance presented, the presence or absence of working examples, and the quantity of experimentation necessary to enable the claims over their full scope. Giving due consideration to all the *Wands* factors, it was concluded that the specification fails to provide an enabling disclosure for the full scope of the claims. Numerous references were provided pointing to the unpredictability in the art of DNA vaccination.

At page 12 of the response, Applicant asserts that the scope of the claims should not be limited to the NMDAR1 antigen because the specification discloses other NMDA receptor subunit families, as well as references that would direct one of skill in the art to further information regarding NMDA receptor subunit families. However, disclosure of other NMDA receptors is not sufficient to enable vaccines that employ nucleic acids encoding these other receptors, which have an intended use of providing a neuroprotective effect, nor to enable methods of producing a neuroprotective effect over a wide variety of neurological injuries and diseases. Given the unpredictability in the art of DNA vaccination, undue experimentation would have been required to use the various NMDA receptor subunits to produce an immune response that is neuroprotective for the enormous variety of diseases covered by the claims.

At page 12 of the response, Applicant asserts that the specification provides guidance for animal models of neurological disorders and further provides guidance for testing additional antigens for use in the claimed invention, to generate antibodies that can cross a compromised blood-brain barrier and modify the function of the selected target receptor. However, the suggestion to go out and test a wide

variety of receptors across an enormous variety of neurological diseases and conditions, given the very large number of parameters that can be varied within the scope of the claims, such as route of administration, dosage, type of vector, etc., and further given the unpredictability in the art of DNA vaccination, for reasons of record, would clearly constitute undue experimentation. The instant specification does not provide specific guidance for predicting which antigens will provide neuroprotection for which diseases, nor does the specification provide specific guidance teaching which conditions will sufficiently compromise the blood-brain barrier (BBB) such that sufficient amounts of antibodies are able to cross and produce the desired effect.

At page 12 of the response, Applicant asserts that one of skill in the art would be familiar with a large number of target receptors associated with neurological disorders and that "it is merely routine experimentation to run the identified target receptors through the claimed methods in order to test their efficacy in treating neurological disorders." No support is offered for this assertion. Given the evidence of record establishing the unpredictability in the art of DNA vaccination, the unsupported assertion that only routine experimentation would be needed to enable the entire scope of the claims is not persuasive. It is not a matter of testing all the possible vaccine formulations against all possible neurological disease models, but of predictably achieving success across the very broad scope of the claims, using nothing more than routine experimentation. Applicants are not claiming a method of identifying a therapeutic vaccine formulation, but rather are claiming methods of actually producing a therapeutic response across a very broad scope of vaccine formulations and therapeutic protocols, in any subject having any neurological condition.

At page 13 of the response, Applicant asserts that the specification sufficiently enables the claims because it provides guidance on routes of administration for the vaccine. However, the guidance provided is in the form of general guidance rather than specific guidance. The specification contemplates that any route of administration used for DNA vaccination can be used to carry out the claimed invention,

including intravenous, subcutaneous, intraperitoneal, or intramuscular. Such guidance constitutes general guidance, not specific guidance. Contemplation of various routes of administration of a vaccine does not constitute enablement for all modes of administration within the context of the claimed invention. Giving due consideration to the Wands factors, the appropriate analysis leads to the conclusion that only oral administration is enabled by the specification.

At page 14 and again at page 17 of the response, Applicant asserts that the animal models of the specification are art-recognized and used for correlating neurological disorders in humans. However, the issue is not whether the animal models accurately model the features of the human disease, but whether the immune response obtained in a rat is predictive of the immune response that would be obtained in other animal species, including humans. The claims are broadly directed to any subject. The rejection of record and the art of record note that the strength and nature of the immune responses to administration of DNA vaccines varies between species and that it is not clear that results from one species are predictive in another (page 10 of the Office Action of 11/21/05). Applicant's response does not address the unpredictability in the art and therefore is not persuasive.

At pages 14-17 of the response, Applicant summarizes the results from the various working examples presented in the specification. These results were acknowledged in the Office Action of 11/21/05. Applicants are reminded that the Examiner has already acknowledged that such embodiments are enabled and that a scope of enablement has already been indicated.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-12, 14-16, 18, and 19 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2, 5, 6, 11, 15, 16, 18, and 19 remain indefinite in their recitation of "neurological disorder." The specification defines a "neurological disorder" as any impairment or absence of a normal neurological function or presence of an abnormal neurological function in a subject (page 10, lines 25-32). This encompasses any change in mental function from a normal state. However, the specification does not define what the normal baseline state is. Therefore, the metes and bounds of the claims cannot be determined.

Claims 12 and 14 have been amended so that they now recite the term "neurological disorder" and therefore are rejected on the same grounds as set forth in the preceding paragraph. This rejection is necessitated by the amendments to the claims.

At page 18 of the response, Applicant states that the metes and bounds of the term "neurological disorder" is clearly defined in the specification at page 38, line 23 through page 39, line 2. On the contrary, the definition is a non-limiting definition which cannot set forth the metes and bounds of claim terminology.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, Claims 2, 5, 6, 12, 14, 15 recites the broad recitation "target protein," and the claim also recites "an N-methyl-D-aspartate (NMDA)

receptor antigen" which is the narrower statement of the range/limitation. The claims have been amended to recite an NMDA receptor antigen. Antibodies elicited by a nucleic acid encoding an NMDA receptor antigen will be specific for the NMDA receptor. Therefore, the produced antibodies will only bind the NMDA receptor, not any other "target protein." This rejection is necessitated by the amendments to the claims.

Claims 12, 14, and 15 are indefinite in their recitation of "ameliorating a neurological disorder in a subject" in the preamble and "to thereby provide neuroprotection to the subject" in the conclusion because the preamble claim language conflicts with the claim language in the conclusion. The term "neuroprotection" includes neuroprotection of healthy subjects and diseased subject, whereas the preamble claim language requires that the subject actually has a neurological disorder, which then must be ameliorated by the method, but the conclusion does not require amelioration of the neurological disorder. The term "neuroprotection" does not require amelioration of an existing deficit. This rejection is necessitated by the amendments to the claims.

Claims 16, 18, and 19 are indefinite in their recitation of "comprising genomic DNA of an N-methyl-D-aspartate (NMDA) receptor antigen" because an NMDA receptor antigen does not contain genomic DNA and therefore the phrase "genomic DNA of an N-methyl-D-aspartate (NMDA) receptor antigen" is indefinite. This rejection is necessitated by the amendment to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 4-8, 10, 16, 18, and 19 stand rejected under 35 U.S.C. 102(a) as being anticipated by Lissin et al. (June 1998).

Lissin et al. disclose an adenovirus that encodes an NMDA receptor (NR1), which is capable of being expressed in cultured hippocampal neurons (abstract, page 7097, Materials and Methods). Thus, the reference teaches all the limitations of the claims as written.

Thus, the prior art anticipates the claimed invention.

At page 19 of the response, Applicant asserts that there is no suggestion that the HA tagged NR1 described by Lissin et al. can be expressed *in vivo* "such that the expressed antigen elicits production of antibodies in a circulatory system of the subject, wherein the antibodies pass across the blood-brain barrier into a central nervous system upon injury." On the contrary, it is well established that when the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent. See MPEP 2112.01 and *In re Best,* 195 USPQ 430, 433 (CCPA 1997). The office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D..

Anne-Marie Falk
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER